

REMARKS

Claims 1-3, 6, and 8-32 are pending in the application. Claims 8-19 were withdrawn from consideration, leaving claims 1-3, 6, and 20-32 subject to examination. Claims 1-3, 6, and 30-32 were rejected under 35 U.S.C. § 112, first paragraph (enablement); claims 1-3, 6, and 20-32 were rejected under 35 U.S.C. § 112, first paragraph (written description); claims 1-3, 6, 20-32 were rejected under 35 U.S.C. § 102(a); and claims 1-3, 6, and 20-32 were rejected under 35 U.S.C. § 103(a). Each of the rejections is addressed below.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-3, 6, and 30-32 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Applicants request reconsideration of this rejection.

Applicants first note that, in the interest of expediting prosecution, claim 1 has been amended herein to specify a method for determining whether the etiology of heart failure in a human test subject may relate to a mutation in a titin gene, involving comparison of the sequence encoded by a titin gene of the subject to the sequence of SEQ ID NO:2. Thus, the claims now specify not only a particular class of heart conditions (heart failure), they also specify the testing of particular human test subjects (those having heart failure), rather than testing a subject to see if they may have such a condition. In addition, the required comparison is very specific: comparison of a test sequence to that of SEQ ID NO:2. Further, Applicants note that the claims are not directed to methods of obtaining a diagnosis for a subject, based on detection of a mutation. Rather, the claims specify methods of determining whether an already existing condition may relate to a titin mutation. If there is not a mutation in the test sequence, then such

a mutation cannot be related to the etiology of the heart failure, while if there is a mutation, there may be a relationship between the mutation and the subject's condition, which is a matter that could be studied further, if desired.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph for lack of enablement be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (written description)

Claims 1-3, 6, and 20-32 were also rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. Applicants respectfully request reconsideration of this rejection.

As discussed above, to expedite prosecution, the claims have been amended to specify methods of determining whether the etiology of heart failure in a human test subject may relate to a mutation in a titin gene. It is not necessary to have information as to which mutations may be associated with heart failure in the application, as merely detecting the presence of a mutation provides useful information. As noted above, detection of a mutation would indicate the possibility of genetic involvement, while the absence of a mutation indicates no such involvement, at the level of the analyzed sequences.

In view of the amendments and remarks set forth above, Applicants respectfully request that the rejection for lack of adequate written description be withdrawn.

Rejections under 35 U.S.C. § 102(a)

Claims 1-3, 6, 20, 21, and 23-31 remain rejected under 35 U.S.C. § 102(a) as being

anticipated by Satoh et al. (Biochem. Biophys. Res. Com. 262:411-417, 1999). In response to Applicants' prior submission with respect to the Declaration of inventor Xiaolei Xu, the Examiner stated that the declaration is insufficient, because (i) the declaration does not state that the acts relied upon to establish that the date prior to the reference were carried out in this country or in a NAFTA country or WTO member country, (ii) the declaration is only submitted by one inventor, but it is unclear whether both inventors invented the subject matter in the claims or which inventor invented the subject matter invented the subject matter in each claim, and (iii) the exhibit was difficult to read and follow, and that an explanation of the relevant steps was not provided in the declaration. With respect to the latter issue, the Examiner cites M.P.E.P. § 715.03 for teaching that "a showing of prior completion of one or a few species within the disclosed genus is generally not sufficient to overcome the referenced or activity." Applicants respectfully request reconsideration of this rejection, as discussed below.

First, Applicants submit herewith a revised declaration, which includes a statement that the acts relied upon in the declaration were carried out in this country. In response to the second consideration noted above, the enclosed new declaration is by both of the inventors. With respect to the third issue, Applicants submit that the exhibit is described in a sufficient manner with respect to the presently claimed invention. As is noted above, in the interest of expediting prosecution, the present claims have been amended to specify comparison of a test sequence to a specific human sequence (SEQ ID NO:2). The declaration shows that the inventors had identified the zebrafish titin gene in zebrafish as that gene including a mutation resulting in the pickwick phenotype. Based on this discovery, and the already known human sequence, the inventors thus discovered a method for determining whether a mutation in a titin sequence may

relate to heart failure by analysis of human titin gene sequences. In view of the above,

Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-3, 6, and 20-32 were rejected under 35 U.S.C. § 102(a) as being anticipated by Siu et al., Circulation 99:1022-1026, 1999. Applicants request that this rejection be withdrawn. The Examiner states that this reference teaches obtaining a nucleic acid-containing sample from a human test subject and amplifying a naturally occurring cardiac specific N2B exon of human titin to determine its sequence. The Examiner further states that the present claims do not actually require detection of a mutation. In response, Applicants note that the present claims now specify detection of a mutation, which is not taught by Siu. Accordingly, this rejection may now be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-3, 6, and 20-32 were rejected under 35 U.S.C. § 103(a) for obviousness over Genbank Accession number X90568, in view of Muller-Seitz et al., Genomics 18:559-561, 1993. In the rejection, the Examiner states, as in the rejection over Siu, that the present claims do not require detection of a mutation. The Genbank reference is cited for teaching the sequence of human titin mRNA, while Muller-Seitz is cited for teaching PCR amplification of the titin gene and sequencing of fragments. Based on these references, the Examiner concludes that it would have been obvious to sequence the titin mRNA. In response, Applicants note that the present claims now specify detection of a mutation in titin sequences, which is not taught or suggested by the cited references. Applicants thus respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. A petition to extend the period for replying to the Office action for 3 months, to and including April 3, 2008, is filed herewith, as well as authorization for payment of the required extension fee. If there are any charges not covered or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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